Andrew Koff et al.

Appl. No. 10/038,060

Amdt. dated March 18, 2005

Reply to Office Communication of March 7, 2005

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

- 1. (Currently amended) A method for increasing the proliferation of thymocytes in a non-human an animal comprising altering an endogenous gene encoding p27^{Kip1} in an isolated thymocyte, or an isolated multipotent cell that differentiates into a thymocyte, of the animal to cause a functional deficiency of cyclin-dependent kinase inhibitor function of p27^{Kip1}, introducing the altered cells having the functional deficiency of cyclin-dependent kinase inhibitor function of p27^{Kip1} to the animal thereby increasing the proliferation of thymocytes in the animal.
- 2. (Previously presented) The method of claim 1, wherein the multipotent cell is a bone marrow cell.
- 3. (Original) The method of claim 1, wherein the animal is a rodent, pig, sheep, frog, or bovine.
- 4. (Previously presented) The method of claim 1, wherein the gene encoding p27^{Kipl} is altered by insertion of a positively selectable marker gene, mutation of the gene encoding p27^{Kipl}, or deletion of the gene encoding p27^{Kipl}.
- 5. (Previously presented) The method of claim 4, wherein the gene encoding p27^{Kipl} is altered by insertion of a positively selectable marker gene into the gene encoding p27^{Kipl}.

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- 6. (Previously presented) The method of claim 5, wherein the positively selectable marker gene encodes neomycin resistance, thymidine kinase, adenine phosphoribosyl transferase, hypoxanthine-guanine phosphoribosyl transferase or dihydrofolate reductase.
- 7. (Previously presented) The method of claim 6, wherein the positively selectable marker gene encodes neomycin resistance.
- 8. (Previously presented) The method of claim 1, further comprising: introducing a plasmid into the insolated cell, wherein the plasmid comprises the gene encoding p27^{Kip1} altered by insertion of a positively selectable marker gene.
- 9. (Previously presented) The method of claim 8, wherein the plasmid further comprises a negatively selectable marker gene adjacent the altered gene encoding p27^{Kip1}, whereby the distance between the negatively selectable marker gene and the altered gene encoding p27^{Kip1} is sufficient to allow homologous recombination between the altered gene encoding p27^{Kip1} and the endogenous gene encoding p27^{Kip1} in the cell.
- 10. (Previously presented) The method of claim 9, wherein the negatively selectable marker gene encodes thymidine kinase.
- 11. (Original) The method of claim 8, wherein the plasmid is delivered to the cell by electroporation, microinjection or transformation.